

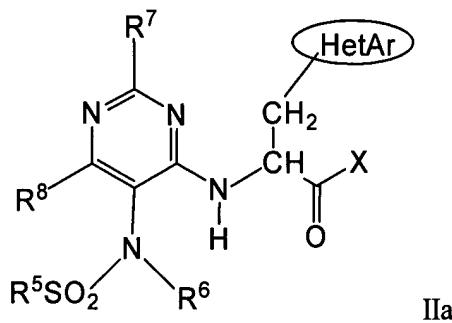
AMENDMENTS

In the claims

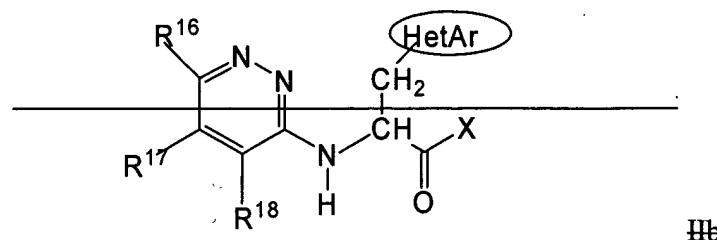
This listing of claims will replace all prior versions and listings of claims in this application.

1-10 (canceled)

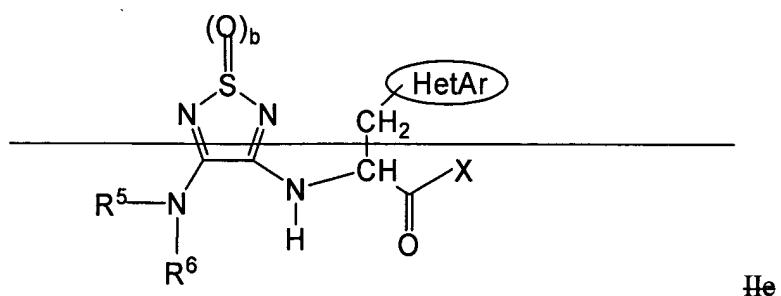
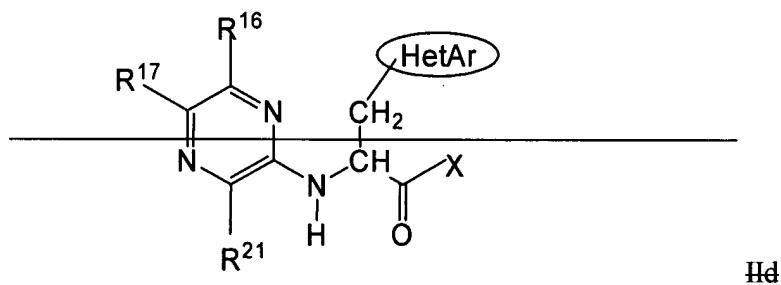
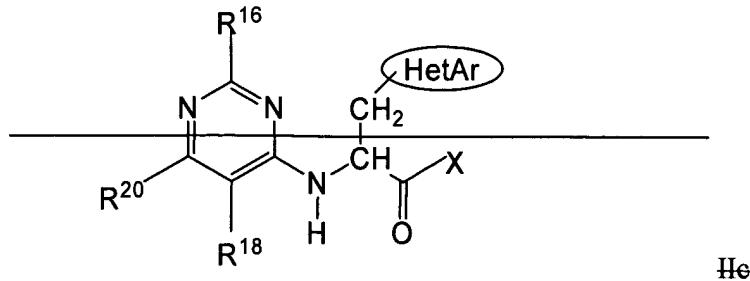
11. (currently amended) ~~The compound of Claim 1 wherein the compound has A compound having the formula IIa, IIb, or IIc, IId, or IIe:~~



IIa



IIb



wherein:

HetAr is a nitrogen containing heteroaryl group substituted with a substituent selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino, aryl, substituted aryl, and oxysulfonyl;

R5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO₂R10 where R10 is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R7 and R8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R16 and R17 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R18 is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and heterocyclic and substituted heterocyclic;

R20 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and heterocyclic, substituted heterocyclic and halogen;

R21 is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

X is hydroxyl; and

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

12. (canceled)

13. (currently amended) The compound of Claim 11 or 12 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with a group of formula -O-Z-NR¹¹R^{11'} or -O-Z-R¹² wherein R¹¹ and R^{11'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO₂-.

14. (original) The compound of Claim 13 wherein the nitrogen containing heteroaryl group is substituted with a group of formula -OC(O)NR¹¹R^{11'} wherein R¹¹ and R^{11'} are independently selected from the group consisting of alkyl or R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle.

15. (original) The compound of Claim 14 wherein the nitrogen containing heteroaryl group is substituted with -OC(O)N(CH₃)₂ and is at the para position of the heteroaryl group.

16. (currently amended) The compound of Claim 11 or 12 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with an aryl or substituted aryl group.

17. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1-9, 11 or 12.

18. (canceled)

19. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 10.

20. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 13.

21. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of 14.

22. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of 15.

23. (withdrawn) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 16.

24. (currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim [[10]] 11.

25. (previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 13.

26. (previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 14.

27. (previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 15.

28. (previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 16.

29. (previously presented) A compound selected from the group consisting of N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-

dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(2,5-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(2-methoxyphenyl)pyridin-2-yl)alanine;

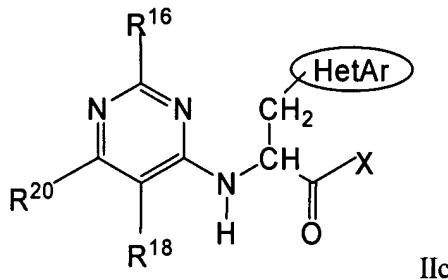
N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(N,N-dimethylamino-carbonyloxy)pyridin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(2-(N,N-dimethylamino-carbonyloxy)pyridin-5-yl)alanine; and

pharmaceutically acceptable salts thereof.

30. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 29.

31. (new) A compound having the formula IIc:



wherein:

HetAr is a nitrogen containing heteroaryl group substituted with a substituent selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino,

aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino, aryl, substituted aryl, and oxysulfonyl;

R16 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R18 is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R20 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and heterocyclic, substituted heterocyclic and halogen;

R21 is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

X is hydroxyl; and

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

32. (new) The compound of Claim 31 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with a group of formula $-O-Z-NR^{11}R^{11'}$ or $-O-Z-R^{12}$ wherein R¹¹ and R^{11'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO₂-.

33. (new) The compound of Claim 32 wherein the nitrogen containing heteroaryl group is substituted with a group of formula $-OC(O)NR^{11}R^{11'}$ wherein R¹¹ and R^{11'} are

independently selected from the group consisting of alkyl and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle.

34. (new) The compound of Claim 33 wherein the nitrogen containing heteroaryl group is substituted with $-OC(O)N(CH_3)_2$ and is at the para position of the heteroaryl group.

35. (new) The compound of Claim 32 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with an aryl or substituted aryl group.

36. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound Claim 31.

37. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound Claim 32.

38. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound Claim 33.

39. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound Claim 34.

40. (new) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound Claim 35.